

## REMARKS

### I. STATUS OF THE CLAIMS

Claims 1-8, 10, 13-26 were cancelled previously. Claim 9 is amended presently, to incorporate salient recitations from claim 12, now cancelled along with claims 30 and 33. Upon entry of the amendments, claims 9, 11, 27-29, 31-32, 34-44 will be pending in the application.

### II. REJECTIONS UNDER 35 U.S.C. § 112, ¶2

The examiner rejects claims 9, 11-12, and 27-44 for alleged indefiniteness. According to the rejection, recitation of the terms “0.2  $\mu\text{m}$ ” and “0.45  $\mu\text{m}$ ” is confusing. Applicant respectfully disagrees. The specification explains how filters of various sizes, such as 0.2  $\mu\text{m}$  and 0.45  $\mu\text{m}$ , can be used in series. So informed, the skilled person would readily appreciate the meets and bounds of the claim terms in question. For example, see ¶¶ 34 and 35 of the published application. Furthermore, applicant has revised claim 9 in a manner believed to obviate the stated ground for rejection.

### III. REJECTIONS UNDER 35 U.S.C. § 103

The examiner rejects claims 9-12 and 27-44 for alleged obviousness over Khatchatourians *et al.* in view of Christen *et al.* Applicant respectfully traverses the rejection.

The examiner understands Khatchatourians to “teach the separation of minicells from normal, contaminating bacterial cells by inducing normal cells to filamentate followed by selective elimination of the filamentous bacteria.” Office Action dated July 25, 2008, at page 6. Applicant explained previously, however, that Khatchatourians’ notion of preparing preparations of minicells is flawed. *See* Response filed March 10, 2008. After Khatchatourians’ 1973 publication, that is, practitioners learned that his assumption was wrong that “sonic treatment disrupts whole cells” and “does not affect minicells.”

In reply the examiner requested “empirical data,” evincing Khatchatourians’ shortcomings. Office Action dated July 25, 2008, pages 4 and 5. Applicant provides such

evidence by way of the accompanying declaration of inventor Himanshu Brahmbhatt (“Second Brahmbhatt Declaration”).

These data clearly show that even mild sonication severely damages intact minicells. *See* Second Brahmbhatt Declaration, ¶ 10 and figure. In particular, sonication at even the lowest energy level for just a few minutes causes minicells and bacterial cells alike to lose membrane integrity and to lyse. In light of the fact that Khatchatourians proposed employing higher sonication levels for up to 2 hours, the skilled artisan, *circa* 2003, would have dismissed the Khatchatourians methodology as an illustration of how *not* to purify bacterial minicells. *Id.* at ¶ 11.

Contrary to the examiner’s assertion, moreover, Christen did not teach the successful isolation of minicells using a 0.45  $\mu\text{m}$  filter. In fact, Christen did not provide any data regarding 0.45  $\mu\text{m}$  filters, and he noted that, “[w]hen Millipore 0.65  $\mu\text{m}$  or 0.45  $\mu\text{m}$  filters were used, very low capacities and/or flow rates were obtained with low yields of minicells, *confirming that such membrane filters are not suitable for preparing substantial quantities of minicells.*” Page 197, 1<sup>st</sup> column (emphasis added). Consequently, Christen actually *taught away* from using 0.45  $\mu\text{m}$  filters to purify minicells. Instead, the reference recommended purifying minicells using a Whatman glass fiber filter (Fisher Scientific 09-874-68), which retains particles down to 0.7  $\mu\text{m}$ . *Id.* at pg. 198 and Appendix 1.

As noted previously, applicant was the first to discover both the size and size uniformity of minicells. *See* First Brahmbhatt Declaration, ¶¶ 10 & 11. By virtue of these discoveries, *inter alia*, applicant formulated the claimed methodology and demonstrated its use for separating minicells from filamentous parent bacterial cells. The result, a composition of minicells characterized by heretofore unattainable levels of purity, was likewise wholly unexpected in view of the contemporaneous literature. *Id.* at ¶ 12.

As presently claimed, therefore, the inventive methodology satisfies a long-felt need, extant some 30 years, for a process of obtaining minicell compositions containing fewer than about 1 contaminating parent bacterial cell per  $10^8$  minicells or less. *Id.* at ¶ 13. Indeed, applicants’ discovery enabled for the first time the production of minicell compositions of

pharmaceutical-grade purity, clearing the way for minicells to advance from the research bench to pharmaceutical applications.

Accordingly, applicant submits that the examiner has not established a *prima facie* case of obviousness, and they request withdrawal of the rejection.

They also request an early indication that this application is in allowable condition. Examiner Lankford is invited to contact the undersigned directly, should he feel that any issue requires further consideration.

The Commissioner is hereby authorized to charge any additional fees, which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, and to credit any overpayment to Deposit Account No. 19-0741. Should no proper payment accompany this response, then the Commissioner is authorized to charge the unpaid amount to the same deposit account. If any extension is needed for timely acceptance of submitted papers, then applicant hereby petitions for such extensions under 37 C.F.R. §1.136 and authorizes payment of the relevant fee(s) from the deposit account.

Respectfully submitted,

*Brian M. Carter*

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By Reg. No. 48,571

FOLEY & LARDNER LLP  
Customer Number: 22428  
Telephone: (202) 672-5404  
Facsimile: (202) 672-5399

For Stephen A. Bent  
Attorney for Applicant  
Registration No. 29,768